

### Claims

1. Method for determining *in vivo* protein activity comprising
  - 5 a) hyperpolarising the NMR active nuclei of samples collected from a human or non-human animate body preadministered with at least one probe compound containing at least one NMR active nuclei and
  - b) analysing said samples by NMR spectroscopy
- 10 2. Method according to claim 1 wherein from said analysis of step b) an NMR pattern I is generated, the method comprises the further steps of
  - c) hyperpolarising the NMR active nuclei of samples collected from a human or non-human animate body preadministered with said at least one probe compound and at least one putative drug,
  - 15 d) analysing said samples by NMR spectroscopy and hereby generating an NMR pattern II,
  - e) comparing the NMR patterns I and II thus identifying distinctions in the NMR pattern II, which are due to the administration of the putative drug.
- 20 3. Method according to claims 1 to 2 wherein at least two probe compounds are selected.
4. Method according to claims 1 to 3 wherein the probe compounds are enriched with NMR active nuclei.
- 25 5. Method according to claims 1 to 4 wherein hyperpolarisation is carried out by means of polarisation transfer from a noble gas, brute force, dynamic nuclear polarisation (DNP) or spin refrigeration.
- 30 6. Method according to claims 1 to 5 wherein the collected samples are biofluids.
7. Method according to claims 1 to 6 wherein said probe compounds are substrates, inducers or inhibitors for Cytochrome P 450 (CYP450)

8. Method according to claim 7 wherein said probe compounds are substrates, inducers or inhibitors for CYP 450 isoenzymes selected from the group consisting of CYP1A2, CYP2A6, CYP2C8/9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4.
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9. Method according to claims 1 to 8 for phenotyping
10. Method according to claims 2 to 8 for studying drug-drug interaction.
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11. Mixture comprising at least two probe compounds, all probe compounds being enriched with  $^{13}\text{C}$ - and/or  $^{15}\text{N}$  NMR active nuclei.
12. Mixture according to claim 11 wherein said mixture comprises at least 3 probe compounds, preferably at least 4 probe compounds.
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13. Mixture according to claims 11 to 12 wherein said probe compounds are probe compounds that interact with proteins selected from the group consisting of NADPH quinone oxireductases, CYP450, N-acetyltransferase, glutathione transferase, thiomethyltransferase, thiopurine methyltransferase, sulfotransferase, UDP-glucuronosyl transferase, pseudocholinesterase, serotonin transport protein, ATP binding cassette (ABC's) and p-glycoprotein.
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14. Mixture according to claims 11 to 13 wherein the mixture comprises probe compounds selected from the group consisting of phenacetin, coumarin, tolbutamide, phenytoin, mephenytoin, S-mephenytoin, bufuralol, chlorzoxazone, midazolam, caffeine, dapsone, diclofenac, debrisoquine, bupropion, antipyrine, dextromethorphan, warfarin, diazepam, alprazolam, triazolam, flurazepam, chlodiazepoxide theophylline, phenobarbital propranolol, metoprolol, labetalol, nifedipine, digitoxin, quinidine, mexiletine, lidocaine, imipramine, flurbiprofen, omeprazole, terfenadine, furafylline, codeine, nicotine, sparteine, erythromycin, benzoylcholine, butrylcholine, paraoxon, para-aminosalicylic acid, isoniazid, sulfamethazine, 5-fluorouracil, trans-stilbene oxide, D-penicillamine, captopril, ipomeanol, cyclophosphamide, halothane, zidovudine, testosterone,
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acetaminophen, hexobarbital, carbamazepine, cortisol, oltipraz, cyclosporin A and paclitaxel.

15. Mixture according to claims 11 to 13 wherein the mixture comprises probe compounds selected from the group consisting of sulfathiazole, dapsone, isoniazid, sulfamethoxazole, hydrazaline, caffeine and procainamide.
16. Mixture according to claims 11 to 13 wherein the mixture comprises probe compounds selected from the group consisting of phenobarbital, oltipraz and 3-methyl-cholanthrene.
17. Mixture according to claims 11 to 13 wherein the mixture comprises probe compounds selected from the group consisting of azathioprine, mercaptopurine and thioguanine.
18. Mixture according to claims 11 to 17 wherein the mixture further comprises at least one putative drug.
19. Use of the mixture according to claims 11 to 17 for the determination of *in vivo* protein activity, preferably for phenotyping.
20. Use of the mixture according to claim 18 for studying drug-drug interaction.
21. Mixture comprising at least two probe compounds, all probe compounds being enriched with  $^{13}\text{C}$  and/or  $^{15}\text{N}$  NMR active nuclei, for use as an agent for determining *in vivo* protein activity.
22. Mixture comprising at least two probe compounds, all probe compounds being enriched with  $^{13}\text{C}$  and/or  $^{15}\text{N}$  NMR active nuclei, for the manufacture of an agent for determining *in vivo* protein activity.
23. Mixture according to claims 21 to 22 wherein the mixture further comprises at least one putative drug.